Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 15 (3—4), pp. 281—285 (1974)

Diabetes insipidus and polycythaemia

By

T. Révész, P. Erdélyi, and Z. Hidvégi

Second Department of Paediatrics, Semmelweis University Medical School, Budapest, and Section of Paediatrics, County Hospital, Cegléd

(Received May 9, 1974)

The case of a fourteen year-old boy suffering from diabetes insipidus and polycythaemia is reported. The possible mechanisms resulting in the association of the two rare disorders are discussed in detail.

Both diabetes insipidus and polycythaemia are conditions infrequent in childhood; their association has not been reported in the literature available to us.

Diabetes insipidus is caused by the failure of the posterior pituitary lobe due in some cases to an injury, infection or tumour affecting this organ or the hypothalamus. Mostly, the cause is unknown and then the condition is termed idiopathic. The disease is characterized by polyuria and polydipsia as the kidneys only excrete urine of a very low specific gravity. Under the effect of exogenous antidiuretic hormone the volume of urine decreases and its specific gravity increases.

Polycythaemia is characterized by a large red blood cell mass due to increased erythrocyte production. Accordingly, the values for erythrocyte count, haematocrit and total erythrocyte volume are higher than normal. Thus, haemoglobin concentration exceeds 16 g per 100 ml,the haematocrit amounts to 55% or more, the erythrocyte count to 6.5 million or more and total red blood cell volume to more than 35 ml per kg body weight. The disease should be differentiated from haemoconcentration and polycythaemia vera. In the latter disorder, which is extremely rare in childhood, white blood cell and platelet counts as well as erythrocyte counts are above normal [1, 14, 17]. Polycythaemia is generally induced by increased erythropoietin production, although the erythropoietin level is not always elevated.

Secondary polycythaemia is induced by prolonged exposure to high altitudes, cardio-pulmonary diseases and other disorders associated with hypoxia of longer duration, renal diseases and endocrine disturbances [4—9, 12, 16, 20, 21].

Report of a Case

P. F., a male patient, was born in 1959 with 2500 g. During infancy he had developed well, started to walk at 14 months, to speak at 18 months. He had been trained at two. At the age of two and half years

the parents had noticed that the child drank much and produced much urine, and was again wetting his bed. Regarding it first as a bad habit, they had often thirsted the boy for hours. The symptoms had failed to improve and in 1962 the child had been taken to a country hospital. There he had been described as a nervous child with dry skin, continuously asking for water. Physical examination revealed no alteration. The child had drunk around 3, and sometimes more than 5, litres of water daily. Urine volume had been accordingly high with a specific gravity of 1004. Upon the administration of intranasal Pitressin[R] snuff, his constant feeling of thirst had declined and urinary output decreased. With the regular use of this drug he had stayed free of symptoms. His plethoric appearance had first been noted at the age of 11 but a full haematological examination had not been done.

In February, 1973, the child was taken to the County Hospital in Cegléd, because of a tetanic seizure. Laboratory investigations revealed the above mentioned two disorders and he was transferred for further investigations to Budapest. On admission the patient was found to lag in growth, of a plethoric appearance; physical examination revealed no other symptoms. He tolerated thirsting with extreme difficulty, but was active and happy with the regular use of Pitressin[R] snuff.

Laboratory Data

Height: 143 cm (−20 cm; below 30 percentile);
Weight: 38.3 kg (−10 kg; below 10 percentile);
Blood pressure: 105/70 mm Hg;
Sedimentation rate: 1 mm/hour;
Haemoglobin: 21.8 g per 100 ml; haematocrit: 65 per cent;
RBC: 6.1 million/μl; WBC: 6000/μl; platelets: 185 000/μl; reticulocytes: 2‰; Hgb F: 1%;
MCV: 106.5 cu.μ (normal, 88 cu.μ); MCH: 35 pg (normal, 27−33 pg); MCHC: 33.5% (normal, 33%);
Erythrocyte volume: 2880 ml (normal: 1500 ml);
Plasma volume: 1580 ml, blood volume: 4400 ml;
Serum protein: 7.0 g per 100 ml; fractions: normal distribution;
Hgb electrophoresis: normal; methaemoglobin: not detectable;
Erythrocyte oxygen affinity:
at pH 7.13, P_{50} = 31.0 mm Hg;
at pH 7.48, P_{50} = 22.5 mm Hg;
Glucose-6-phosphate-dehydrogenase: 21.5 Δ OD/min/g Hgb; 2,3-DPG: 13.9 μM/g Hgb; pyruvate kinase: 1.57 ΔOD/min/g Hgb $\times 10^4$;
Erythrocyte ATP: 0.89 μM/ml red blood cell;
Erythrocyte half life (r of ^{51}Cr-labelled red cells), in the patient: 29 days, in normal donor: 29 days (normal: 25−35 days);
Erythrocyte sequestration:
spleen sequestration index: 62;
liver: 50 (normal: 20−60);
Leukocytic alkaline phosphatase activity: 109 (normal: 50−150);
Bone marrow;
myeloid : erythroid ratio = 2 : 1;
myeloblast: 8%; promyelocyte: 8%; myelocyte: 16%; metamyelocyte: 10%; band: 10%; neutrophile granulocyte: 38%; lymphocyte: 10%; normoblast: 43%; megaloblast: 11%;
X-rays of thorax, skull and abdomen revealed nothing pathological;
ECG, EEG, respiratory functions: normal values;
Serum bilirubin: 0.8 mg per 100 ml; thymol turbidity: 1 Unit; 17-ketosteroid excretion: 6.1 mg/24 hours;
Urine: protein, sugar, acetone: not detectable; urobilinogen: normal; specific gravity: 1004;
Concentrating capacity: see Table I;
Serum creatinine: 1.4 mg per 100 ml;
Endogenous creatinine clearance: 20 ml/min/1.73 sq.m;
Erythropoietin: 0.08 Unit (below normal);
Renal ^{131}I-hippuran scan: normal.

TABLE I

Concentrating capacity tests in patient P. F.

	Before testing	After thirsting	After the injection of 5 mg Pitressin tannate	Normal values
Specific gravity	1000	1002	1010	>1025
Serum osmolality (mosm/l)	292	312	295	290–300
Urine osmolality (mosm/l)	93	93	360	> 900
Serum osmolality (mosm/l)	0.32	0.29	1.21	4.25

DISCUSSION

The laboratory findings left no doubt that the child was suffering from both diabetes insipidus and polycythaemia. Although unable to produce concentrated urine on thirsting, he did so under the effect of Pitressin tannate, thus ruling out the possibility of a nephrogenic diabetes insipidus. However, even with Pitressin^{R}, the concentrating capacity was impaired, and in spite of the normal plasma creatinine level and renal scan, the clearance of creatinine was repeatedly less than normal.

The haematological findings were indicative of polycythaemia, while the isolated increase of erythropoietic activity in the bone marrow and the normal leukocytic alkaline phosphatase activity excluded the possibility of polycythaemia vera [1, 14, 17].

No signs of hypoxia were found and respiratory functions were normal. Methaemoglobinaemia, haemoglobinopathies and cardio-vascular disease were ruled out. The absence of symptoms in the family excluded the possibility of a benign familial erythrocytosis [3, 19].

There are several data in the literature concerning the occurrence of polycythaemia in association with endocrine disorders [2, 6, 7, 10, 12, 16] but to our best knowledge polycythaemia associated with diabetes insipidus has not been described before. Cushing's syndrome is well-known to be accompanied by polycythaemia, but other syndromes such as the overproduction of androgens [7], phaeochromocytoma [2], primary aldosteronism [16], diabetes mellitus and diencephalic lesions [11] can also be complicated by polycythaemia.

The association of renal disease with polycythaemia is well documented. Tumours [4, 21], polycystic kidney [20], nephrocalcinosis [5], hydronephrosis [9, 18] may induce erythrocytosis. In some of these disorders, the erythropoietin level is increased. On the other hand, polycythaemia in itself may cause renal disturbances [15]. In this case, renal function is impaired as a consequence of the high haematocrit and blood viscosity. This

mechanism may have been responsible for the reduction of creatinine clearance observed in our patient.

Classification of the polycythaemia found in our patient proved to be difficult. There were signs pointing to an endocrine origin, notably the diabetes insipidus, retarded growth, a lower than normal plasma 17-ketosteroid value. Although in the child's history there are no data indicative of some hypothalamic or pituitary injury, bleeding or infection, the possibility of a slight, subclinical lesion still remains. This in turn could have caused both diabetes insipidus and later polycythaemia.

Another possibility for the explanation of the polycythaemia lies in the causative role of a renal disorder. Repeated exposures to thirsting, as told by the parents, could easily have affected the kidneys, thus stimulating them for increased erythropoietin production [13]. We have, however, failed to demonstrate an elevated erythropoietin level. Whatever the exact mechanism, the association of the two rare disorders has prompted us to report the case.

Acknowledgement

The authors are indebted to Dr. A. Vidos, and to Dr. J. Török, for information concerning the patient's history; and to Dr. I. Fehér for erythropoietin determinations.

References

1. Aggeler, P. M., Pollycove, M., Hoag, S., Donald, W. G., Lawrence, J. H.: Polycythemia vera in childhood. Studies of iron kinetics with Fe^{59} and blood clotting factors. Blood **17,** 345 (1961).
2. Bradley, J. E., Young, J. D., Lentz, D.: Polycythemia secondary to pheochromocytoma. J. Urol. (Baltimore) **86,** 1 (1961).
3. Auerbach, M. L., Wolff, J. A., Mettier, S. E.: Benign familial polycythemia in childhood. Pediatrics **21,** 54 (1958).
4. Conley, C. L., Kowel, J., D'Antonio, J.: Polycythemia associated with renal tumors. Bull. Johns Hopkins Hosp. **101,** 63 (1957).
5. Cöster, C.: Renal polycythaemia. Acta med. scand. **197,** 2 (1961).
6. Daughaday, W. H., Williams, R. H., Daland, G. A.: The effect of endocrinopathies on the blood. Blood **3,** 1342 (1948).
7. Donati, R. M., Gallagher, N. I.: Haematologic alterations associated with endocrine disease. Med. Clin. N. Amer. **52,** 231 (1968).
8. Gallo, R. C., Fraimow, W., Cathcart, R. T., Erslev, A. J.: Erythropoietic response in chronic pulmonary disease. Arch. intern. Med. **113,** 559 (1964).
9. Gardner, F. H., Freymann, J. G.: Erythrocythaemia and hydronephrosis. New Engl. J. Med. **259,** 323 (1958).
10. Gold, A. P., Michael, A. F. Jr.: Congenital adrenal hyperplasia associated with polycythemia. Pediatrics **23,** 727 (1959).
11. Halvorsen, S.: The central nervous system in regulation of erythropoiesis. Acta haemat. (Basel) **35,** 65 (1966).
12. Haynal, I., Gráf, F.: The role of the hypophyseal-hypothalamic system in the pathogenesis of erythraemia and symptomatic polycythaemia. Acta med. scand. **139,** 61 (1950).
13. Husband, P., Howlett, K. A.: Renal papillary necrosis in infancy. Arch. Dis. Childh. **48,** 116 (1973).
14. Knock, H. L., Githins, J. H.: Primary erythrocytosis of childhood. Amer. J. Dis. Child. **100,** 189 (1960).
15. Malizia, G.: Renal function and haemodynamics in primary and secondary polycythaemia. Acta med. scand. **154,** 5 (1956).
16. Mann, D. L., Gallagher, N. I., Donati, R. M.: Erythrocytosis and primary aldosteronism. Ann. intern. Med. **66,** 335 (1967).
17. Marlow, A. A., Fairbanks, V. F.: Polycythemia vera in an eleven year old girl. New Engl. J. Med. **263,** 950 (1960).

18. Mitus, W. J., Toyama, K., Brauer, M. J.: Erythrocytosis, juxtaglomerular apparatus (JGA) and erythropoietin in the course of experimental hydronephrosis in rabbits. Ann. N. Y. Acad. Sci. **149,** 107 (1968).
19. Moden, B.: Benign erythrocytosis. Brit. J. Haemat. **375,** 14 (1968).
20. Rosse, W. F., Waldmann, T. A., Cohen, P.: Renal cysts, erythropoietin and polycythemia. Amer. J. Med. **34,** 76 (1963).
21. Thorling, E. B., Ersbak, J.: Erythrocytosis and hypernephroma. Scand. J. Haemat. **1,** 38 (1969).
22. Williams, W. J., Beutler, E., Erslev, A. J., Rundles, R. W. (Eds): Hematology. McGraw-Hill, New York 1972, p. 544.

Dr. T. Révész
Tűzoltó u. 7.
H-1094 Budapest, Hungary